

(12) INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(19) World Intellectual Property  
Organization  
International Bureau



(43) International Publication Date  
4 March 2004 (04.03.2004)

PCT

(10) International Publication Number  
WO 2004/018624 A3

(51) International Patent Classification<sup>7</sup>: A61K 39/02,  
C07H 21/04, C12P 21/02, C12N 1/21, 15/74, C07K 14/31

(21) International Application Number:  
PCT/US2003/025879

(22) International Filing Date: 20 August 2003 (20.08.2003)

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data:  
60/404,406 20 August 2002 (20.08.2002) US

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(81) Designated States (national): AE, AG, AL, AM, AT, AU,  
AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU,  
CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH,  
GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC,  
LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW,  
MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC,  
SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA,  
UG, US, UZ, VC, VN, YU, ZA, ZM, ZW.

(84) Designated States (regional): ARIPO patent (GH, GM,  
KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW),  
Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM),  
European patent (AT, BE, BG, CH, CY, CZ, DE, DK, EE,  
ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO,  
SE, SI, SK, TR), OAPI patent (BF, BJ, CF, CG, CI, CM,  
GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG).

**Published:**

- with international search report
- before the expiration of the time limit for amending the  
claims and to be republished in the event of receipt of  
amendments

(88) Date of publication of the international search report:  
25 November 2004

For two-letter codes and other abbreviations, refer to the "Guid-  
ance Notes on Codes and Abbreviations" appearing at the begin-  
ning of each regular issue of the PCT Gazette.

(54) Title: RANDOM TRANSPOSON INSERTION IN STAPHYLOCOCCUS AUREUS AND USE THEREOF TO IDENTIFY  
ESSENTIAL GENES

(57) Abstract: The invention provides a method for generating a database of candidate essential genes in *Staphylococcus aureus*, as well as otherwise important genes that, when mutated, lead to a growth attenuated phenotype. Such genes and mutants of such genes are important for identifying antibacterial agents suitable for treating and preventing *S. aureus* infections. The invention includes methods for confirming the essentiality or importance of candidate genes, as well as methods for utilizing those genes to screen for new antibacterial drugs. The invention also includes the antibacterial agents identified using the disclosed methods, as well as methods of using the same for treating and preventing *Staphylococcus* infection.

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# INTERNATIONAL SEARCH REPORT

International application No.

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## A. CLASSIFICATION OF SUBJECT MATTER

IPC(7) : A61 K 39/02 ; C07 H 21/04 ; C12 P 21/02 ; C12 N 1/21,15/74 ; C07 K 14/31  
US CL : 424/190.1, 200.1; 45/69.3, 252.3, 320.1; 530/350; 536/23.1, 23.7

According to International Patent Classification (IPC) or to both national classification and IPC

## B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)  
U.S. : 424/190.1, 200.1; 45/69.3, 252.3, 320.1; 530/350; 536/23.1, 23.7

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)  
Please See Continuation Sheet

## C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	US 5,962,222 A( KADERBHAI ) 05 October 1999 (05.10.1999) SEQ.ID.NO:2 from position 1 to 2675.	1-3,20-24 and 37-41(in part)

☐ Further documents are listed in the continuation of Box C.

☐ See patent family annex.

\* Special categories of cited documents:

"A" document defining the general state of the art which is not considered to be of particular relevance

"E" earlier application or patent published on or after the international filing date

"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art

"&" document member of the same patent family

Date of the actual completion of the international search

18 September 2004 (18.09.2004)

Date of mailing of the international search report

01 OCT 2004

Name and mailing address of the ISA/US

Mail Stop PCT, Attn: ISA/US

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# INTERNATIONAL SEARCH REPORT

International application No.

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## Box I Observations where certain claims were found unsearchable (Continuation of Item 1 of first sheet)

This international report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☐ Claim Nos.:  
because they relate to subject matter not required to be searched by this Authority, namely:
  
2. ☐ Claim Nos.:  
because they relate to parts of the international application that do not comply with the prescribed requirements to such an extent that no meaningful international search can be carried out, specifically:
  
3. ☐ Claim Nos.:  
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

## Box II Observations where unity of invention is lacking (Continuation of Item 2 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:  
Please See Continuation Sheet

1. ☐ As all required additional search fees were timely paid by the applicant, this international search report covers all searchable claims.
2. ☐ As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
3. ☐ As only some of the required additional search fees were timely paid by the applicant, this international search report covers only those claims for which fees were paid, specifically claims Nos.:
  
4. ☒ No required additional search fees were timely paid by the applicant. Consequently, this international search report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.: 1-3, 20-24, 37-41 ( in part )

Remark on Protest ☐ The additional search fees were accompanied by the applicant's protest.  
☐ No protest accompanied the payment of additional search fees.

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### BOX II. OBSERVATIONS WHERE UNITY OF INVENTION IS LACKING

This application contains the following inventions or groups of inventions 1-7 which are not so linked as to form a single general inventive concept under PCT Rule 13.1. In order for all inventions to be examined, the appropriate additional examination fees must be paid.

Group 1 Claim(s) 1-3, 20-24, 37-41 (in part) drawn to an isolated nucleic acid molecule encoding a polypeptide having at least 80% identity to a polypeptide encoded by a nucleic acid sequence selected from the group consisting of *S. aureus* open reading frames listed in Table 1, library of nucleic acid, vector and a host cell.

Group 2 Claim (s) 4-12 (in part) drawn to a method for screening for an antimicrobial agent using bacterial gene.

Group 3 Claim (s) 13-19 (in part) drawn to a method for evaluating a test agent for inhibition of expression of the gene of *S. aureus*.

Groups 4 Claim (s) 25-28 (in part) drawn to a protein.

Groups 5 Claim (s) 29-32 and 34 (in part) drawn to an antibody or agent.

Group 6 Claim (s) 33, 35, and 36 (in part) drawn to a method of treating or protecting *S. aureus* infection using antibody or agent.

Group 7 Claim (s) 42-57 (in part) drawn to a method for identifying a library of putative essential genes, genes, antimicrobial agent and pharmaceutical composition.

The inventions listed as Groups 1-7 do not relate to a single general inventive concept under PCT Rule 13.1 because, under PCT Rule 13.2, they lack the same or corresponding special technical features for the following reasons:

Group 1, claim(s) 1-3, 20-24, 37-41 are drawn to an isolated nucleic acid molecule encoding a polypeptide encoded by a nucleic acid sequence selected from the group consisting of *S. aureus* open reading frames listed in Table 1 which is the first product.

Pursuant to PCT Rule 13.2 the ISA/US considers that where multiple products, processes and methods are claimed, the main invention shall consist of the first invention of the category first mentioned in the claims and the first recited invention of each of the other categories related thereto. Accordingly the main invention (Group 1) comprises the first product.

Further pursuant to PCT Rule 13.2 the ISA/US considers that any feature which the subsequently recited products and methods share with the main invention does not constitute a special technical feature within the meaning of PCT Rule 13.2 and that each of such products and methods accordingly defines a separate invention. Therefore, the groups of inventions below do not constitute a special technical feature within the meaning of PCT Rule 13.2 and that each of such products and methods accordingly defines a separate invention.

NOTE: It is not clear to the Office whether SEQ.ID.NOS submitted in the electronic version are which open reading frames of the Table 1. Table 1 contains several hundreds of genes but they are not identified by sequence identification numbers. There is no paper copy of the sequence listing in the application. However, the electronic copy appears to contain only 13

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sequences of which only SEQ.ID.NO: 11, 12 and 13 appear to contain open reading frames. Therefore, the search will be carried out using only SEQ.ID.NO: 11.

The inventions listed as Groups 1-7 do not relate to a single general inventive concept under PCT Rule 13.1 because, under PCT Rule 13.2, they lack the same or corresponding special technical features for the following reasons:

The technical feature linking groups 1-7 appears to be that they all relate to nucleic acid encoding polypeptides that have sequence identity to polypeptide encoded by nucleic acid sequence of *S.aureus*.

However, U.S. Patent 5962222 disclose an isolated nucleic acid SEQ.ID.NO: 2, encoding polypeptide that is 88.2% identical to the polypeptide encoded by nucleic acid SEQ.ID.NO: 11. Therefore, the technical feature the linking the inventions 1-7 does not constitute a special technical feature as defined by PCT Rule 13.2 as it does not define a contribution over the prior art.

The technical feature of Group 1 is considered to be a nucleic acid encoding a polypeptide.

The technical feature of Groups 2 is considered to be a method for screening for an antimicrobial agent using bacterial gene.

The technical feature of Group 3 is considered to be a method for evaluating a test agent for inhibition of expression of the gene of *S.aureus*.

The technical feature of Group 4 is considered to be a protein.

The technical feature of Group 5 is considered to be an antibody or agent.

The technical Group 6 is considered to be a method of treating or protecting *S. aureus* infection using agent or antibody.

The technical Group 7 is considered to be method for identifying a library of putative essential genes, genes, antimicrobial agent and pharmaceutical composition.

### Continuation of B. FIELDS SEARCHED Item 3:

MEDLINE, STN, A -GENSEQ, N-GENSEQ, EST, DERWENT, SWISS-PROT, PIR, USPTOWEST, SWISSPTREMBL, GENEMBL, PUBLISHED APPLICATIONS AND ISSUED PATENTS